Intensive Care Med
https://doi.org/10.1007/s00134-026-08366-w

UNDERSTANDING THE DISEASE

Cardiac output and determinants

Sulagna Bhattacharjee[1*], Ricard Ferrer[2] and Olfa Hamzaoui[3,4]

© 2026 Springer-Verlag GmbH Germany, part of Springer Nature

Understanding cardiac output (CO) physiology is essential in intensive care, as it directly guides the management of shock and tissue oxygen delivery. CO, defined as the volume of blood ejected per minute, equals stroke volume (SV) multiplied by heart rate (HR). The cardiac index (CI), which adjusts CO for body surface area, more accurately reflects cardiac performance and normally ranges between 2.5 and 4.0 L/min/m^2 [1]. CO depends on intrinsic cardiac factors (HR and contractility) and vascular determinants (preload and afterload), whose dynamic interaction ensures effective heart–vascular coupling.

Intrinsic determinants of CO:

Heart rate

The Bowditch effect, also known as the staircase or Treppe phenomenon, is a force–frequency relationship, where increasing stimulation frequency increases contractility, by increasing cytosolic calcium concentration and myofilament sensitivity to calcium [2]. However, two physiological constraints limit the magnitude of HR augmentation: (1) tachycardia shortens diastole, thereby reducing myocardial perfusion and oxygen supply [3]; (2) excessive tachycardia increases oxygen demand and can compromise cardiac performance. This mechanism explains why excessive tachycardia may impair CO and provides a physiological rationale for HR control in selected clinical situations, particularly when diastolic filling becomes the limiting factor. Emerging evidence also suggests that vagal afferent signaling may impose a "ceiling effect" on maximal HR to protect against myocardial ischemia, further underscoring the limited role of HR in enhancing CO [4].

*Correspondence: bhattacharjee.sulagna85@gmail.com; drsulagna@aiims.edu
[1] Department of Anaesthesiology, Pain Medicine & Critical Care, All India Institute of Medical Sciences, New Delhi, India
Full author information is available at the end of the article

Contractility

Myocardial contractility is defined as the intrinsic ability of the myocardium to generate force and shorten at a given preload and afterload, independent of loading conditions [5]. It depends on intracellular calcium influx, formation of troponin–actin–myosin complexes, and ATP-mediated relaxation [6]. Contractility also adapts to loading changes: increased preload augments stroke volume via the Frank–Starling mechanism, whereas acute afterload elevation induces an immediate stretch response followed by the slower Anrep effect, helping to preserve cardiac output [7]. End-systolic elastance derived from pressure–volume loop analysis remains the gold standard for assessing intrinsic contractility in research settings. In the intensive care unit (ICU), however, this invasive approach is impractical, and echocardiography is the preferred bedside tool for evaluating systolic function and guiding inotropic and fluid therapy [6].

Stroke volume

Stroke volume (SV), defined as the difference between left ventricular end-diastolic and end-systolic volumes, is determined by preload, afterload, and contractility. A preserved SV reflects effective ventriculo-arterial coupling [6]. Beyond forward flow, part of SV is temporarily stored in the proximal aorta during systole and released during diastole, ensuring continuous organ perfusion. This elastic buffering function is described by the two-element Windkessel model. Within this physiological framework, the relationship between SV and pulse pressure can be expressed through simplified indices such as arterial compliance (SV/pulse pressure) or arterial stiffness (pulse pressure/SV) [8]. Classic physiological studies further showed that CO can remain stable across a wide range of HR through compensatory adjustments in SV, highlighting the dominant role of SV regulation under most conditions. However, at extreme HR values, heart rate becomes a critical determinant of CO [9]. In adults,

SHOUT
SHARE
IT

the normal stroke volume index (SVI) ranges from 35 to 65 mL/m^2. In critically ill patients, particularly those with shock, reduced SVI is associated with worse outcomes. Jentzer et al. [10] demonstrated that an SVI < 35 mL/m^2 independently predicts increased hospital mortality, emphasizing its prognostic significance.

Extrinsic determinants of CO:

Preload and its determinants

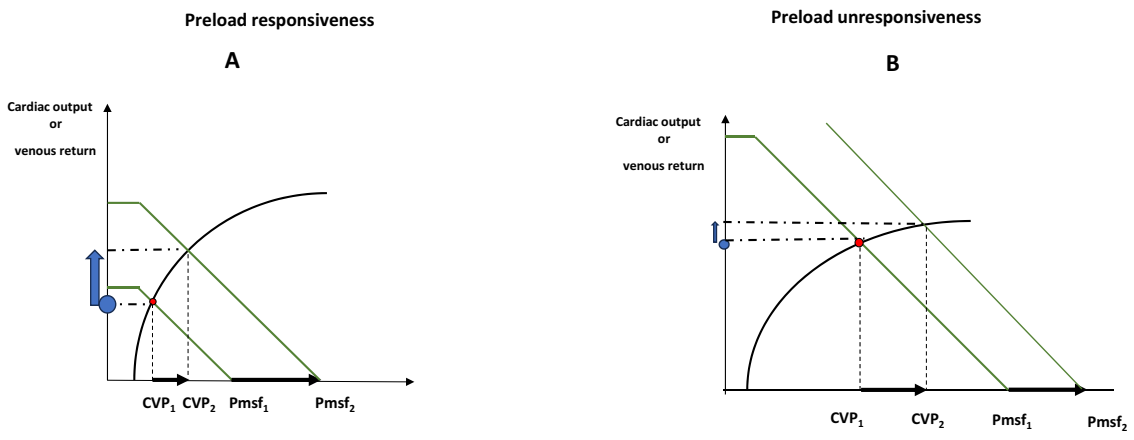
Preload refers to myocardial fiber stretch at end-diastole and determines stroke volume through the Frank–Starling (FS) mechanism. Although clinically approximated by end-diastolic volume or filling pressures, these surrogates do not always reflect true myocardial stretch [11]. Conceptually, preload represents ventricular filling within compliance limits, whereas preload reserve denotes the capacity to further increase stroke volume in response to enhanced venous return [12].

Venous return (VR), preload, venous tone, and FS mechanism

The cardiovascular system functions as a closed loop in which venous return (VR) equals cardiac output (CO) at equilibrium. Changes in VR modulate CO via the FS mechanism [11]: increased preload optimizes actin–myosin interaction, augmenting stroke volume. Once maximal fiber stretch is reached, however, the ventricle becomes preload unresponsive and further increases in filling no longer raise stroke volume. The RAP at which the two functions intercept indicates the functioning preload of the RV, the back pressure for VR, and the CO. Because VR and CO are equal at steady state, their curves can be plotted on the same graph. Their intersection defines the hemodynamic operating point, while the mean systemic filling pressure (Pmsf)—the x-intercept of the VR curve—represents the upstream driving pressure for venous return (Fig. 1). With constant venous tone, Pmsf varies proportionally with total blood volume through changes in stressed blood volume (SBV). However, venous tone independently modulates SBV: venoconstriction shifts blood from the unstressed to the stressed compartment, increasing Pmsf without altering total blood volume, whereas venodilation produces the opposite effect [13]. The effects of different treatment modalities on the hemodynamic variables are illustrated in Figs. 1 and 2.

Afterload and its determinants

Afterload is the total wall stress the ventricle must overcome during systolic ejection and, when acutely increased, tends to decrease SV and CO unless compensated by contractile adaptation. According to Laplace's law, wall tension (T) is proportional to pressure (P)



CVP$_1$ & **CVP$_2$** -central venous pressure values; **Pmsf$_1$** & **Pmsf$_2$** -mean systemic filling pressure values; Frank-Starling curve-black; venous return curves-green.

Fig. 1 Fluid infusion increases Pmsf in all patients. (**A** *X* axis represents right atrium pressure and *Y* axis venous return or cardiac output). Fluid infusion leads to a marked rise in mean systemic filling pressure (Pmsf) and a slight increase in central venous pressure (CVP), resulting in an increased venous return gradient and, consequently, higher venous return and cardiac output (CO). This occurs when the heart operates on the steep portion of the Frank–Starling (FS) curve. (1B *X* axis represents Right atrium pressure and *Y* axis venous return or Cardiac output). Fluid infusion produces a marked rise in mean systemic filling pressure (Pmsf), but also a substantial increase in central venous pressure (CVP), leaving the venous return gradient unchanged. As a result, venous return and cardiac output (CO) do not increase. This situation corresponds to the heart functioning on the flat portion of the Frank–Starling (FS) curve

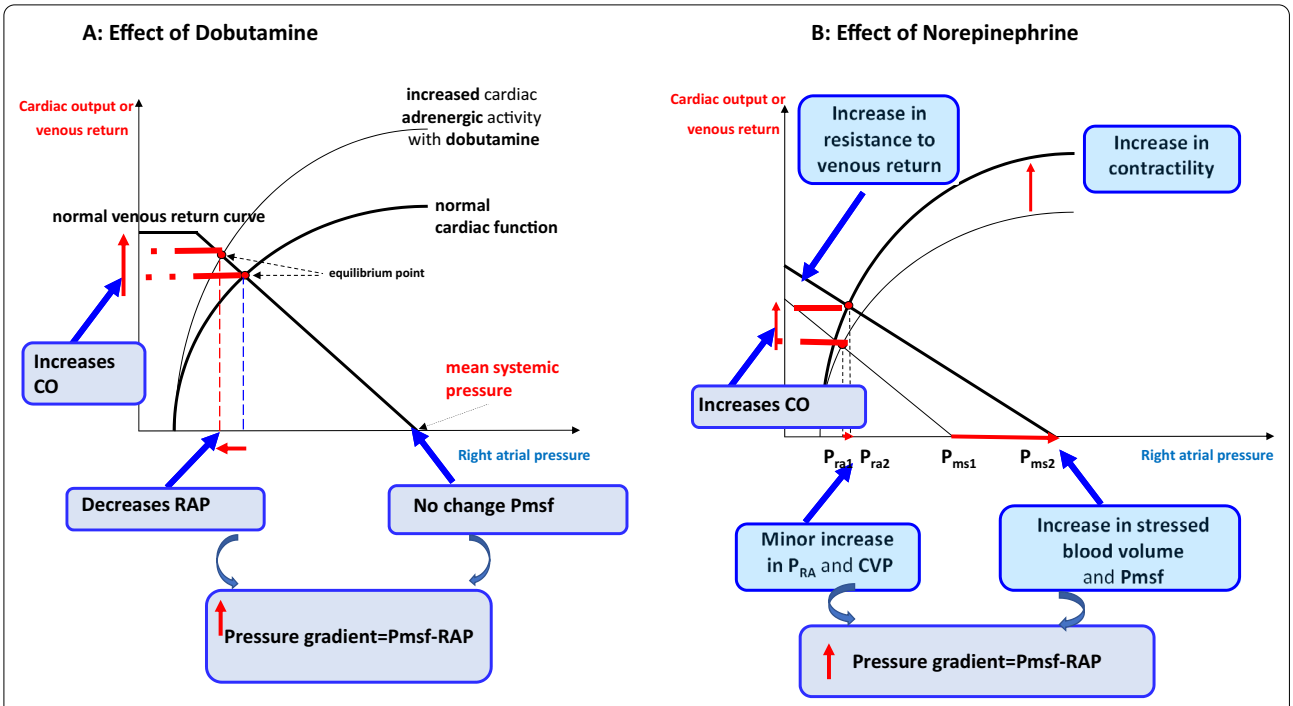


Fig. 2 **A** (*X* axis represents the right atrium pressure and *Y* axis the venous return or cardiac output). Effect of dobutamine: inotrope-like dobutamine increases cardiac output (CO) by enhancing myocardial contractility, which lowers right atrial pressure (RAP) and thereby widens the pressure gradient between mean systemic filling pressure (Pmsf) and RAP, leading to an increase in venous return and overall cardiac output. **B** (*X* axis represents the right atrium pressure and *Y* axis the venous return or cardiac output). Effect of norepinephrine: vasopressor like norepinephrine redistributes blood from the unstressed to the stressed volume, thereby raising Pmsf and increasing VR gradient, despite increased resistance to VR and afterload, thereby improving CO through greater preload, enhanced contractility (β1 effect), and higher coronary perfusion

and radius (r), and inversely related to wall thickness (h): $T=P\times r/2h$. Clinically, afterload reflects vascular resistance, arterial impedance, ventricular geometry, and transmural pressure [14]. In the absence of outflow obstruction, left ventricular end-systolic pressure approximates 0.9×aortic systolic arterial pressure (SAP), making systolic pressure a major determinant of afterload. Because direct aortic pressure measurement is rarely available, peripheral SAP is commonly used as a pragmatic—though indirect—surrogate of left ventricular afterload in ICU patients [15].

The way forward

Optimizing CO in critical illness requires an individualised approach to target the hemodynamic variables of preload, afterload, HR and contractility, for navigating a delicate balance of providing circulatory support with therapeutic interventions like fluid, vasopressors and inotropes, against the risks of overloading the heart or vasculature, with the ultimate goal of ensuring effective organ perfusion.

Abbreviations

CO: Cardiac output; HR: Heart rate; SV: Stroke volume; PP: Pulse pressure; ICU: Intensive care unit; VR: Venous return; FS: Frank–Starling; Pmsf: Mean systemic filling pressure; LVSEP: Left ventricular end-systolic pressure; SAP: Systolic arterial pressure; Zin[w]: Aortic input impedance.

Author details

[1] Department of Anaesthesiology, Pain Medicine & Critical Care, All India Institute of Medical Sciences, New Delhi, India. [2] Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain. [3] Unité de Médecine Intensive et Réanimation Polyvalente, CHU Reims, Reims, France. [4] Université de Reims Champagne-Ardenne, UR 3801 PPF, Reims, France.

Declarations

Conflicts of interest

The authors have no conflict of interest to declare. RF is a Deputy Editor for Intensive Care Medicine. He has not taken part in the review or selection process of this article.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 16 November 2025 Accepted: 25 February 2026
Published online: 09 March 2026

References

1. Reddy YNV, Melenovsky V, Redfield MM, Nishimura RA, Borlaug BA (2016) High-output heart failure: a 15-year experience. J Am Coll Cardiol 68:473–482
2. Palomeque J, Vila Petroff MG, Mattiazzi A (2004) Pacing staircase phenomenon in the heart: from Bodwitch to the XXI century. Heart Lung Circ 13:410–420
3. Heinonen I (2025) Cardiac output limits maximal oxygen consumption, but what limits maximal cardiac output? Exp Physiol 110:666–674
4. Boushel R, Calbet JA, Radegran G, Sondergaard H, Wagner PD, Saltin B (2001) Parasympathetic neural activity accounts for the lowering of exercise heart rate at high altitude. Circulation 104:1785–1791
5. Muir WW, Hamlin RL (2020) Myocardial contractility: historical and contemporary considerations. Front Physiol 11:222
6. Pagel Paul SBBT, Tawil Justin N, Freed Julie K (2024) Cardiac physiology. In: Kaplan JA, Augoustides JG, Manecke GR (eds) Kaplan's cardiac anesthesia: perioperative and critical care management. Elsevier, Philadelphia, pp 119–153
7. Cingolani HE, Perez NG, Cingolani OH, Ennis IL (2013) The Anrep effect: 100 years later. Am J Physiol Heart Circ Physiol 304:H175–H182
8. Chemla D, Hebert JL, Coirault C, Zamani K, Suard I, Colin P, Lecarpentier Y (1998) Total arterial compliance estimated by stroke volume-to-aortic pulse pressure ratio in humans. Am J Physiol 274:H500–H505
9. Guyton AC, Sagawa K (1961) Compensations of cardiac output and other circulatory functions in areflex dogs with large A-V fistulas. Am J Physiol 200:1157–1163
10. Jentzer JC, Wiley BM, Anavekar NS, Pislaru SV, Mankad SV, Bennett CE, Barsness GW, Hollenberg SM, Holmes DR Jr, Oh JK (2021) Noninvasive hemodynamic assessment of shock severity and mortality risk prediction in the cardiac intensive care unit. JACC Cardiovasc Imaging 14(2):321–332
11. Berlin DA, Bakker J (2015) Starling curves and central venous pressure. Crit Care 19:55
12. Magder S (2016) Volume and its relationship to cardiac output and venous return. Crit Care 20:271
13. Fudim M, Kaye DM, Borlaug BA, Shah SJ, Rich S, Kapur NK, Costanzo MR, Brener MI, Sunagawa K, Burkhoff D (2022) Venous tone and stressed blood volume in heart failure: JACC review topic of the week. J Am Coll Cardiol 79(18):1858–1869
14. Norton JM (2001) Toward consistent definitions for preload and afterload. Adv Physiol Educ 25:53–61
15. Bertrand M, Goury A, Chemla D, Teboul JL, Hamzaoui O (2025) Applied physiology at the bedside: using invasive blood pressure as a true monitoring tool. Ann Intensive Care 15(1):192